IE 400 Principles of Engineering Management

Project

Group 34
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PART A

Decision Variables:

- x_1: Dosage of Melphalan
- x_3: Dosage of Decitabine
- x_4: Dosage of Pentostatin
- x_7: Dosage of Thiotepa

Since we are only allowed to make dose changes for the existing ingredients in the base regiment, only the drugs in the base regimen are included as decision variables.

Objective Function:

- $max\ 0.28x_1 + 0.25x_3 + 0.17x_4 + 0.40x_7 - 34$

The goal is to maximize the quality of life of the patient, thus the objective function is maximizing the Q-score formula.
From the patient's characteristics $p = (0, 0, 0, 1, 0, 0, 1, 1, 1)$ we get constant -14.
From the drugs included $y = (1, 0, 1, 1, 0, 0, 1)$ we get constant -20.
From the drug dosages $x = (x_1, 0, x_3, x_4, 0, 0, x_7)$ we get
$0.28x_1 + 0.25x_3 + 0.17x_4 + 0.40x_7$.
When we sum up everything in the Q-score formula we get the formula in the objective function.

Constraints:

- $x_1 + x_2 + x_3 + x_4 = 100$: An acceptable chemotherapy regimen is 100cl.
- $x_1 \geq 20$: Min Dose of Melphalan
- $x_1 \leq 80$: Max Dose of Melphalan
- $x_3 \geq 20$: Min Dose of Decitabine
- $x_3 \leq 100$: Max Dose of Decitabine
- $x_4 \geq 10$: Min Dose of Pentostatin
- $x_4 \leq 100$: Max Dose of Pentostatin
- $x_7 \geq 20$: Min Dose of Thiotepa
- $x_7 \leq 50$: Max Dose of Thiotepa

Cplex Output:
Obj Value: 32.3
Values of Decision Variables: [20.0, 20.0, 10.0, 50.0]

Solution:
Only decision variables were included in CPLEX, since -34 is constant and can be added to the solution manually. Thus, the actual objective value is $32.3 - 34 = -1.7$.

Values of decision variables are:

- $x_1 = 20$
- $x_3 = 20$
- $x_4 = 10$
- $x_7 = 50$

The treatment should include 20cl Melphalan, 20 cl Decitabine, 10cl Pentostatin, 50cl Thiotepa.

PART B

Decision Variables:

- x_i, $i = \{1, 2, 3, 4, 5, 6, 7\}$: Dosage of drug at index i.
- y_i, $i = \{1, 2, 3, 4, 5, 6, 7\}$, $y_i \in \{0, 1\}$: Inclusion of drug at index i.

Parameters:

- $d_1 = |20 - x_1|$
- $d_3 = |30 - x_3|$
- $d_4 = |15 - x_4|$
- $d_7 = |35 - x_7|$

  d_1, d_3, d_4, d_7 represent the dose difference of drugs indexed 1, 3, 4, 7 from the base regimen. Dose difference of drugs that are not present in the base regimen (2, 5, 6) will just be equal to their dosages (x_2, x_5, x_6), thus, absolute valued parameters for those are not needed.

  d_1, d_3, d_4, d_7 will be linearized in the constraints.
- $r_1 = 1 - y_1$
- $r_3 = 1 - y_3$
- $r_4 = 1 - y_4$
- $r_7 = 1 - y_7$

  r_1, r_3, r_4, r_7 represent the removal of drugs indexed 1, 3, 4, 7. Since y_i is binary, r_1, r_3, r_4, r_7 are also binary. Drugs that are not present in the base regimen (2, 5, 6) do not have r parameters, since they can not be removed anyways.
- $Q = -14 - 5y_1 - 6y_2 - 4y_3 - 4y_4 - 8y_5 - 6y_6 - 7y_7 + 0.28x_1 + 0.30x_2 + 0.25x_3 + 0.17x_4 + 0.31x_5 + 0.246x_6 + 0.40x_7$

  This parameter is simply the Q-score formula with patient's characteristics $p = (0, 0, 0, 1, 0, 0, 1, 1, 1)$ values.

Objective Function:

- $min\, d_1 + 2x_2 + d_3 + 3d_4 + 2x_5 + x_6 + d_7$
  $+ 25r_1 + 50y_2 + 10r_3 + 25r_4 + 20y_5 + 30y_6 + 40r_7$
  This objective function is minimizing the unit cost of dosage change and fixed cost of adding/removing drugs using the coefficients from the table given in the project document.

Constraints:

- $20 - x_1 \leq d_1$
- $x_1 - 20 \leq d_1$
- $30 - x_3 \leq d_3$
- $x_3 - 30 \leq d_3$
- $15 - x_4 \leq d_4$
- $x_4 - 15 \leq d_4$
- $35 - x_7 \leq d_7$
- $x_7 - 35 \leq d_7$
  All of the given constraints above are for linearizing the absolute value functions d_1, d_3, d_4, d_7 to be included in the objective function.
- $x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 = 100$: An acceptable chemotherapy regimen is 100cl.
- $x_1 \geq 20y_1$: Min Dose of Melphalan
- $x_1 \leq 80$: Max Dose of Melphalan
- $x_2 \geq 10y_2$: Min Dose of Oxaliplatin
- $x_2 \leq 50$: Max Dose of Oxaliplatin
- $x_3 \geq 20y_3$: Min Dose of Decitabine
- $x_3 \leq 100$: Max Dose of Decitabine
- $x_4 \geq 10y_4$: Min Dose of Pentostatin
- $x_4 \leq 100$: Max Dose of Pentostatin
- $x_5 \geq 10y_5$: Min Dose of Epirubicin
- $x_5 \leq 70$: Max Dose of Epirubicin
- $x_6 \geq 20y_6$: Min Dose of Lomustine
- $x_6 \leq 90$: Max Dose of Lomustine
- $x_7 \geq 20y_7$: Min Dose of Thiotepa
- $x_7 \leq 50$: Max Dose of Thiotepa

- $Q \geq 35$: Quality of life threshold given for the patient
- If $x_i > 0$ then $y_i = 1$: If we have a positive dosage of any drug, then we must have included it in the regimen, so their inclusion value y_i must be 1. This constraint is linearized as follows:
    - $x_i \geq 0.0001 - M(1 - t)$
    - $x_i \leq Mt$
    - $1 - M(1 - t) \leq y_i \leq 1 + M(1 - t)$
    - $1 - Mt \leq y_i \leq 1 + Mt$

      where M is a very large number and $t \in \{0, 1\}$

  From the previous if-then statement, new constraints are added:
- $x_i + M(1 - t) \geq 0.0001$
- $x_i - Mt \leq 0$
- $-M(1 - t) - y_i \leq -1$
- $-M(1 - t) + y_i \leq 1$
- $-Mt - y_i \leq 0$
- $-Mt + y_i \leq 0$

Cplex Output:
At first, the output was:
CPLEX Error 1217: No solution exists.
In order to get a solution, I increased dosage constraint by 10cl until I got a feasible problem. The minimum regimen I got was 230cl.
So the $x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 = 100$ constraint became

$$x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 = 230.$$

With this change, the output was:
Obj Value: 215.00000000000003
Values of Decision Variables: [80.0, 0.0, 100.0, 0.0, 0.0, 0.0, 50.0, 1.0, -0.0, 1.0, -0.0, -0.0, -0.0, 1.0, 60.000000000000014, 70.00000000000003, 15.0, 15.0, 0.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 0.0, 0.0, 1.0, 0.0, 1.0, -0.0, 1.0, 1.0, 1.0, -0.0]
['X1', 'X2', 'X3', 'X4', 'X5', 'X6', 'X7', 'Y1', 'Y2', 'Y3', 'Y4', 'Y5', 'Y6', 'Y7', 'D1', 'D3', 'D4', 'D7', 'R1', 'R3', 'R4', 'R7', 'T1', 'T2', 'T3', 'T4', 'T5', 'T6', 'T7', 'T1not', 'T2not', 'T3not', 'T4not', 'T5not', 'T6not', 'T7not']

Solution:
The objective value is 215. This is the minimum cost of the new regimen with the given constraints. The values of decision variables are:

- $x_i = (80, 0, 100, 0, 0, 0, 50)$
- $y_i = (1, 0, 1, 0, 0, 0, 1)$

The treatment should include 80cl Melphalan, 100cl Decitabine, 50cl Thiotepa.

PART C

As prompted in the project document, this part will build on the model on part b. Nothing is removed or modified, only some additions are made.

New Constraints:

If both Melphalan and Oxaliplatin is included, then their combined dosage must be less than 70cl and greater than 50cl. In mathematical terms:

If $y_1 = 1 \; and \; y_2 = 1$,

Then $50 \leq x_1 + x_2 \; and \; x_1 + x_2 \leq 70$.

Linearizing this constraint, we get:

$y_1 + y_2 - 1 \leq Mk$

$x_1 + x_2 - 50 \leq M(1 - k)$

$x_1 + x_2 + 70 \leq M(1 - k)$

where M is a very large number and $k \in \{0, 1\}$. Thus the new constraints are:

- $y_1 + y_2 - Mk \leq 1$
- $x_1 + x_2 - M(1 - k) \leq 50$
- $x_1 + x_2 - M(1 - k) \leq -70$

Either Epirubicin should be included in the regimen or the dosage of Decitabine should be less than 25cl. In mathematical terms:

Either $y_5 = 1$,

Or $x_3 \leq 25$

Linearizing this constraint, we get:

$x_3 - 25 \leq Ml$

$1 - y_5 \leq M(1 - l)$

where M is a very large number and $l \in \{0, 1\}$. Thus the new constraints are:

- $x_3 - Ml \leq 25$
- $-M(1 - l) - y_5 \leq -1$

If both Pentostatin and Lomoustine are included in the regimen, then at least one of the Thiotepa and Epirubicin should also be chosen. In mathematical terms:

If $y_4 = 1 \; and \; y_6 = 1$,

Then $y_7 = 1 \; or \; y_5 = 1$.

Linearizing this constraint, we get:

$y_4 + y_6 - 1 \leq Mj$

$$1 - (y_5 + y_7) \leq M(1 - j)$$

where M is a very large number and $j \in \{0, 1\}$. Thus the new constraints are:

- $y_4 + y_6 - Mj \leq 1$
- $-y_5 - y_7 - M(1 - j) \leq -1$

Cplex Output:

Again, at first, the output was:

CPLEX Error 1217: No solution exists.

In order to get a solution, I increased dosage from 230cl to 250cl.

So the $x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 = 230$ constraint became

$$x_1 + x_2 + x_3 + x_4 + x_5 + x_6 + x_7 = 250.$$

With this change, the output was:

Obj Value: 274.9999999999999

Values of Decision Variables: [80.00000000000001, 0.0, 100.00000000000003, 0.0, 19.999999999999943, 0.0, 50.0, 1.0, 0.0, 1.0, -0.0, 1.0, 0.0, 1.0, 60.000000000000014, 70.00000000000003, 14.999999999999979, 15.0, 0.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, 0.0, 1.0, -0.0, 1.0, 0.0]

['X1', 'X2', 'X3', 'X4', 'X5', 'X6', 'X7', 'Y1', 'Y2', 'Y3', 'Y4', 'Y5', 'Y6', 'Y7', 'D1', 'D3', 'D4', 'D7', 'R1', 'R3', 'R4', 'R7', 'T1', 'T2', 'T3', 'T4', 'T5', 'T6', 'T7', 'T1not', 'T2not', 'T3not', 'T4not', 'T5not', 'T6not', 'T7not', 'J', 'K', 'L', 'Jnot', 'Knot', 'Lnot']

Solution:

The objective value is 275. This is the minimum cost of the new regimen with the given constraints. The values of decision variables are:

- $x_i = (80, 0, 100, 0, 20, 0, 50)$
- $y_i = (1, 0, 1, 0, 1, 0, 1)$

The treatment should include 80cl Melphalan, 100cl Decitabine, 20cl Epirubicin, 50cl Thiotepa.